

TROPICAL OR AMOEBIC ABSCESS OF THE LIVER AND ITS RELATIONSHIP TO AMOEBIC DYSENTERY.

*Being a Contribution to a Discussion in the Section of
Tropical Diseases at the Annual Meeting of the British Medical
Association at Manchester, July-August, 1902.*

BY

LEONARD ROGERS, M.D., M.R.C.P., F.R.C.S., B.S., I.M.S.,
Officiating Professor of Pathology, Medical College, Calcutta.

IN spite of recent advances it may be safely said that the pathology of tropical abscess of the liver is still in a very confused state. This is well illustrated in the two articles in Clifford Allbutt's *System of Medicine*, the first entitled Suppurative Hepatitis by Davidson, and the second on Amoebic Abscess of the Liver, by Lafleur. The former writer regards the disease as one produced by ordinary pyogenic organisms acting on a liver predisposed to inflammatory changes by life in the tropics, while the latter holds that about half the cases of the disease are associated with amoebae, which act either as direct excitants of pus formation, or only as carriers of pyogenic organisms. Still more divergent are the different views held as to the relationship of liver abscess to dysentery, Manson quoting various writers as having found from 3 to 98 per cent. so connected, this wide divergence no doubt being due to different forms of dysentery being met with in various places; the amoebic form, which is now pretty generally considered to be that which is most intimately connected with liver abscess, constituting a very different proportion of the total cases of dysentery met with in various countries. The intrusion of the amoeba into this field has necessarily upset old ideas as to the pathology of liver abscess, while the number of observations yet recorded has not been sufficient to establish the exact limitations of the played rôle by the new factor, Kartulis's paper, for example, being based on 13 cases, and that of Kruse and Pasquale on 15, in 6 of which only was the amoeba found, the others being classed as "idiopathic."

There are few places where liver abscess can be better studied than at the Medical College, Calcutta, for the state-

ment sometimes made that natives rarely suffer from the disease is totally erroneous as applied to India. Two years ago, while acting as pathologist for a few months at this hospital, I found that, although the thick pus of a liver abscess was often free from amoebae, yet if a scraping of the wall was examined they could always be found quite easily. On returning to the same post with a fair prospect of at least a year's incumbency, I determined to follow up this inquiry by means of a new method in order to get a larger number of cases than necropsies afforded. At my request, my surgical colleagues very kindly obtained for me at the time of opening liver abscesses some of the pus in one sterile test tube, and in another one a small scraping of the wall of the abscess with a Volkmann's spoon. Amoebae were sought for in this material, and at the same time cultures were made on agar tubes for micro-organisms, and the pus was frequently stained for them as well. Between the clinical and *post-mortem* observations over 30 cases have been now examined, and the results have been so uniform that I think conclusions may safely be drawn from them as far as the ordinary clinical form of liver abscess as met with in India is concerned. I am greatly indebted to the kindness of the following officers of the Indian Medical Service: Drs. R. D. Murray, R. H. Charles, D. M. Moir, and R. Bird, Surgeons to the Medical College Hospital, for so supplying me with material from their cases, and to Drs. G. Bamford and G. T. A. Harris, Physicians to the hospital, for permission to examine the cases in those wards.

Advantage has also been taken of the abundant material and records to inquire into the relationship of the disease to dysentery. For this purpose the clinical notes of the cases referred to above, and 92 other cases treated during the last four years in this hospital have been examined, and the histories obtained compared with the lesions found *post mortem*, in order to see how frequently either a history of dysentery or lesions in the bowels are found in cases which it is possible to follow up to the end. As here again the results obtained have been remarkably constant, I have further spent much labour in examining the records of over 5,000 necropsies performed at the Calcutta Medical College in the course of the last twenty-nine years, and have analysed over 200 cases of liver abscess, in many of which an abstract of the clinical records was also available, in order to see how far this large number would support the conclusions derived from the smaller number of carefully-investigated cases to be tabulated in this paper. This mass of material presents many points of interest, but in the present communication I only propose to deal with it from the point of view of the frequency and type of the dysentery met with in association with tropical liver abscess.

THE CONSTANCY OF THE AMOEBA IN TROPICAL LIVER ABSCESS.

The first point to be dealt with is the frequency of the amoeba in tropical liver abscess, by which term I mean the large single or multiple abscess which is clinically recognizable as such during life, as opposed to multiple small pyaemic ones on the one hand, and on the other the rare form of supuration throughout the bile ducts, known as suppurative cholangitis, which is nearly always due to gall stones (having been so caused in 18 out of 20 cases which I collected some years ago, the other 2 having been due to a primary cancer of



TABLE I.—*Liver-Abscess Cases examined Microscopically at the Time of Operation.*

Number.	Caste.	Sex.	Age.	Alcoholism.	Dysentery.	Duration of Illness.	Range of Temperature.	Amoeba in Pus.	Amoeba in Scrapings of Abscess Walls.	Staphylococci in Pus on Culture.	Result.
1	H	M	34	Yes	6 months ago	4 months	98.0° to 100.0°	No	Yes	Yes	Died.
2	H	M	45	No	2 years ago	1½ months	98.0° to 102.0°	Yes	Yes	—	Recovered.
3	H	M	30	Yes	Nil.	1 month	99.0° to 100.4°	No	Yes	No	Recovered seventh day after opening.
4	M	M	35	No	11 months ago (not recorded.)	7 months	97.6° to 100.2°	No	Yes	Yes	Died.
5	H	M	35	No	11 months ago for 5 months	7 months	98.0° to 101.0°	No	Yes	Nil.	Died.
6	H	M	38	No	2 years ago	2 months	98.0° to 100.0°	No	Yes	Yes	Recovered.
7	H	M	44	No	2 years ago	36 days	97.0° to 100.0°	No	Yes	Yes	Recovered.
8	H	M	40	Yes	4 years ago	2 months	Normal	No	Yes	Nil.	Recovered.
9	H	M	24	Yes	Nil.	1 month	—	—	Yes	Nil.	Died.
10	M	M	66	No	1½ month ago	11½ months	100.0° to 103.0°	No	Yes	Nil.	Died.
11	M	M	25	(Clinical notes not available)				No	Yes	Yes	
12	H	M						No	Yes	Nil.	
13								No	Yes	Nil.	
14								No	Yes	Nil.	
15	H	M	35	No	4 months ago (not recorded)	10 days	98.4° to 99.6°	—	Yes	Nil.	Recovered ninth day after opening.
16	H	M	35	Yes	Nil.	1½ month	98.4° to 101.0°	No	Nil.	Yes	Recovered fourth day after opening.
17	H	M	40	Yes				—	Yes	Yes	Recovered twelfth day after opening.
<i>Cases in which the Liver-Abscess Pus only was Examined.</i>											
1	H	M	17	No	2 years ago	20 days	97.8° to 100.0°	No	—	Nil.	
2	M	M	40	Yes	7 years ago	4 months	98.0° to 100.0°	No	—	Nil.	
3	H	M	40	No	2 months ago	8 days	98.0° to 100.4°	Yes	—	Nil.	
4	M	M	28	No	Nil.	4 months	98.0° to 100.2°	No	—	Nil.	
5	H	M	22	Yes	—	2 months	98.0° to 100.2°	No	—	Nil.	
6				(Notes not available)				Yes	—	Yes	
7	H	M	30	No	Not noted	26 days	99.2° to 100.6°	No	—	Nil.	
8	H	M	45	—	For 1 year	2 months	Normal	Yes	—	Nil.	Recovered third day after opening.

H = Hindu; M = Mahomedan.

the bile duct in one, and to a hydatid opening into the duct in the other). These latter forms are rarely, if ever, diagnosed definitely during life, nor are they as yet amenable to surgical treatment as the tropical form nearly always is. Perihepatic abscesses are occasionally met with clinically, but they are nearly always secondary to a primary large abscess of the liver. Owing to the considerable number of cases to be dealt with it will be most convenient to tabulate them so as to bring out clearly the most important points, and to avoid a wearisome record of details of each separate case.

In Table I the cases which have been examined at the time of the operation, or when the case was dressed within the following few days are given. In the first 17 cases a scraping from the wall of the abscess received in a sterile test tube was examined, and in 14 of them some pus in another tube taken at the same time was also examined for amoebae. In the 8 cases at the foot of the table pus only was obtained. In 12 of the first 17 cases the scraping was obtained at the time the abscess was opened, and in all of them amoebae were easily found, nearly always in the first slide examined. On the other hand, out of 14 cases in which pus was obtained at the same time, together with the 8 cases in which the pus only was examined, making 22 in all, in only 4 was the amoeba found, although more trouble was taken over examining the pus than over the scrapings. Possibly they might have been found somewhat oftener in the pus if a still longer amount of time had been spent over examining it, but even then they would not have been detected in the great majority of the cases, while by examining a scraping obtained at the time of the operation, they can always be easily detected. Further, in 5 more cases scrapings were obtained from the wall of the abscess cavity some days after the abscess had been opened, and at the time the wound was being dressed. In 4 of these, which were examined on the third, fourth, seventh, and ninth days respectively, amoebae were readily found in an active condition, but in the fourth, which was examined on the twelfth day, when only a little thin discharge, quite different in character from the typical thick pus discharged from a liver abscess when first opened, was obtainable no amoebae could be found. They may very likely have been present at an earlier date, and this case is of interest when taken in conjunction with No. 2 in Table II (p. 846), in which no amoebae could be found in the wall of a liver abscess *post mortem*, it having been opened fourteen days before death, but in which amoebae were found in chronic ulcers in the caecum. These two cases merely show that the amoebae may disappear from an abscess which has been opened for some days and has been discharging freely, and in no way invalidate the evidence adduced as to the constant presence of this organism in cases of liver abscess of the large "tropical" variety when first opened. If now we turn to Table II, in which are shown 20 cases of this form of liver abscess, whose walls were examined for amoebae *post mortem*, we once more find that they were always found with the solitary exception of Case 2 already explained. If then we exclude, for the reason given, the two cases which were not examined until twelve to fourteen days after the abscess was opened, we have no fewer than 35 consecutive cases in which the amoeba was found in scrapings from the wall of the abscess cavities, that is, at the seat of the active disease process.

We have next to consider if there is any other morbid factor, such as pyogenic organisms in constant or frequent association with "tropical" liver abscess, which could produce wholly, or in part, the pathological changes met with. In this connexion we have to deal with the common pyogenic organisms, which are still regarded by many if not by most writers on the subject as the essential cause of the disease, even if they may sometimes be carried to the liver by means of the amoeba. Turning again to Table I we find out of 24 cases in which cultures were made from the pus of liver abscess cases in only 8 were staphylococci found, and in 2 of these only one or two colonies developed, which may have been accidental contaminations. In the other 5 many colonies were obtained, and in 2 of these cocci were also found in stained specimens of the pus. In the case in which only one colony developed no cocci could be found on staining the pus. In 1 case a short oval bacillus was obtained, which was very possibly a contamination. In the remaining 15 cases the pus proved to be sterile. Turning to Table II we find that cultures were made in 13 cases, and staphylococci were found in 8 of them—streptococci being also found in 1, in which there was a suppurating wound in the leg altogether apart from the amoebic abscess in the liver, from which the streptococci might very possibly have been derived. In 8 out of these 13 cases the abscess had been opened during life, and in 6 of these staphylococci were found, in 1 which had been aspirated only, none were found, while in 4 which had not been operated on cocci were found in 2. Taking the whole number in both tables we have 37 cases with cocci in 16, including 6 cases in which the abscess had been opened with the possibility of infection from without taking place, as undoubtedly occurs sometimes in these cases in spite of every precaution, owing to the inveterate curiosity of the native leading him to disturb his dressings with a most exasperating levity. Including these cases, we find that the cocci of suppuration were found in fewer than half the cases, while in the pus from just opened abscesses they were obtained in only one-third. Moreover, even when present, they may not always be virulent and capable of producing pus, for in one experiment, in which liver abscess pus containing both amoebae and staphylococci were injected into the liver of a cat, no abscess resulted, yet the cocci were recovered from both the scar of the puncture mark in the liver and from the heart blood on killing the animal after his temperature had been normal for some days after a preliminary elevation. Pyogenic organisms, then, are only exceptionally found in active liver abscesses, and when present are not necessarily virulent and capable of producing pus.

We conclude from the above data, then, that the amoeba is the only constantly found organism in "tropical" or amoebic abscess of the liver, as I think it would be more correctly called; and this leads on to the inquiry into the frequency of the association of dysentery with liver abscess, and as to the type of dysentery so related. The kind of dysentery present, whether the ordinary form, which is being traced to Shiga's bacillus with increasing frequency—this organism having been found by me recently in a few cases of ordinary catarrhal dysentery in Calcutta, and serum reactions having been obtained with it—or the amoebic form of the disease, which I have now repeatedly found in liver abscess cases, and in them only as a rule. The great rarity of liver abscess in dysentery

TABLE II.—*Liver-Abscess Cases examined Post Mortem.*

Number.	Caste.	Sex.	Age.	Alcoholism.	Dysentery.	Duration of Illness.	Range of Temperature.	Amoebae in Abscess Wall.	Staphylococci on Culture.	Number of Abscesses Post Mortem	Lesions of Dysentery Post Mortem.
1	H	M	50	Yes	Nil	8 days	97° to 100°	Yes	—	1 large	Ulcers.
2	H	F	30	No	Nil	1½ month	98° to 103°	No*	—	1 large	Chronic amoebic.†
3	H	M	40	Yes	10 years ago	1½ month	98.8° to 100°	Yes	—	1 large	Chronic amoebic with old scars.
4	H	M	30	Yes	(History not recorded)	1 month	98° to 99°	Yes	—	1 large	Scars of recent ulcers in colon.
5	H	M	36	Yes	Nil	1 month	98.4° to 103°	Yes	No	1 large	Nil.
6	H	M	25	Yes	(No note)	1 month	99° to 101°	Yes	No	1 large	Nil.
7	H	M	30	No	22 days ago	19 days	97° to 100°	Yes	Yes**	1 large and 2 small	Congestion and old scars in colon.
8	M	M	30	Yes	2 months ago	20 days	98° to 102°	Yes	Yes	1 large	Ulcers and scars in colon.
9	H	M	40	Yes	In hospital	1 month	98° to 102°	Yes	Yes	1 large	Amoebic dysentery.†
10	H	M	25	Yes	Nil	1 month	98° to 101°	Yes	Yes	1 large	Amoebic dysentery.†
11	H	M	40	No	Nil	1 month	98.8° to 102°	Yes	Yes	1 large	Scars and ulcers in caecum.
12	H	M	23	—	(History not recorded)	1 month	98° to 100.6°	Yes††	Yes	1 small, 1 in lung	Amoebic dysentery.†
13	H	M	45	Yes	30 years ago in hospital	20 days	99° to 101°	Yes	No	3 medium	Ulcers in colon.
14	H	M	60	Yes	For 3 months	20 days	96.6° to 97.6°	Yes	—	—	—
15	M	M	23	Yes	2 years ago.	—	98° to 101°	Yes	No	3 large	Amoebic dysentery.†
16	H	M	26	Yes	(Admitted for fractured femur)	2 months	98° to 101°	Yes	Yes	4 large	Scars of recent dysentery.
17	M	M	6	No	5 years ago and recently	2 months	98° to 101°	Yes	Yes	1 large	Amoebic dysentery.†
18	E	M	38	—	Nil	1 month	97.6° to 98°	Yes	No	1 large	Nil.
19	H	M	22	Yes	2 months ago	1½ month	99° to 100°	Yes	—	1 large	Amoebic dysentery.†
20	H	M	22	—	2 months ago	1½ month	99° to 100°	Yes	—	1 large	Amoebic dysentery.†

* The abscess had been opened and drained for 14 days before death.

† Numerous active amoebae were found in the ulcers in the large intestine.

†† The amoebae were found in the wall of a secondary abscess in the lung.

** Active amoebae were also found in a scraping of the abscess wall at the operation two days before death.

cases (often termed "colitis") in temperate climates, in the epidemic dysentery of armies and in Indian gaols, where only one case of liver abscess is met with in every 620 cases of dysentery, clearly shows that all forms of this disease of the large bowel are not commonly associated with suppurative hepatitis. If, however, "tropical" or amoebic abscess of the liver is only associated with amoebic dysentery, and not with the common form of temperate climates, armies in the field, and that so frequently met with in European asylums and Indian gaols, then all these difficulties will disappear. In order to prove this thesis, it will be necessary to show (1) that dysentery is present at some time or other in a very large proportion of liver abscess cases, and cannot certainly be excluded in the remainder; (2) that the dysentery precedes in date the onset of the liver abscess symptoms; and (3) that the dysentery of tropical or amoebic liver abscess is of the amoebic variety. These three points will now be considered in the order given in the light of the material already mentioned, the data of the cases which I have personally investigated, and which have, as far as possible, been embodied in the tables already given, being first considered, and the conclusions derived from them tested in the light of the larger number of clinical and *post mortem* records which I have analysed.

THE FREQUENCY OF THE ASSOCIATION OF DYSENTERY WITH LIVER ABSCESS.

A brief examination of the columns headed "Dysentery" and "Lesions of Dysentery *Post Mortem*" shows that in the majority of the cases there was both a history of previous dysentery, sometime upwards of a year before, and also lesions of this disease in the large bowel *post mortem*. In other cases, such as Nos. 1, 2, 10 and 11 of Table II, there was no history of dysentery, yet lesions of the disease were found *post mortem*, and were, moreover, of the amoebic variety. It is evident, then, that clinical data alone will not afford correct information as to the proportion of cases in which dysenteric lesions are actually present in the large bowel. Nor will *post-mortem* records alone suffice, for in Nos. 2, 5, and 6 of Table III dysentery was present clinically, at quite recent dates in two of them, and yet no lesions of the large and small bowel or other source of liver infection was found *post mortem*, so that it is evident that it is only by the examination of a series of cases in which both clinical and *post-mortem* records are available, that the true proportion of cases in which dysentery is associated with liver abscess can be ascertained. In order to get a larger series of cases than is provided in Table II, a third table has been compiled from the Medical College Hospital records, in which all the remaining cases of the last four years not included in Table II, in which both clinical and *post-mortem* records are available, are entered. Owing to the notes having been taken by native students they are unfortunately not all complete, the history of the case not having been written up in some of them, while in others no record has been made as to whether the patient had suffered from dysentery or not. Omitting such incomplete cases, we have remaining in Tables II and III 24 cases³ in which

³ The last four cases in Table II were added after the following figures were worked, and owing to one of them showing no history or *post mortem* history of dysentery this class is raised from 4.17 to 7.41 per cent.

the presence or absence of a previous history of dysentery has been recorded, and necropsies subsequently made. In 14, or 58.33 per cent. of these, there was both a previous history of dysentery, and lesions of the disease were found *post mortem*. In 6 more, or 25 per cent., there was no history of previous dysentery, although this had been inquired for, but lesions of the disease were found *post mortem*. In 3 more, or 12.5 per cent., there was a previous history of dysentery, but no lesions were found *post mortem*, showing that the disease may subside and leave no marked naked-eye evidence of its previous existence. In the remaining one case there was neither a history of dysentery or lesion *post mortem*, as must necessarily happen sometimes, even if the disease has been previously present, owing to the occasionally mild or latent form of amoebic dysentery, giving rise to no marked symptoms during life and healing without leaving naked-eye changes before death. Indeed, taking into account the carelessness and forgetfulness of natives with regard to previous illnesses it is very surprising that either a history of the disease or lesions *post mortem* have been recorded in as large a proportion as the 95.83 per cent. in this series of cases, and the evidence strongly points to dysentery being an invariable accompaniment of the amoebic or tropical liver abscess in Calcutta.

The number of cases, however, is too small to allow of final conclusions being drawn from them on such a vexed question as that under consideration, so we must turn to the *post-mortem* records for further evidence on the point. Owing to an abstract of the clinical histories of all cases being entered in the older *post mortem* records of the Calcutta Medical College Hospital a large amount of invaluable material is available for examination, while the fact that these records are mainly by that admirable physician and pathologist, the late Dr. J. F. P. McConnell, greatly enhances their worth. In this series the clinical data are necessarily less complete than the original ward notes, so that we should not expect to find quite so high a proportion of histories of dysentery as in the smaller series discussed above. The total number of cases of the large single or multiple liver abscess under consideration in which the clinical abstracts recorded whether dysentery had been present or not during life which I have been able to analyse amount to 39. Both a previous history of dysentery and lesions *post mortem* were found in 21, or 53.85 per cent. of the cases. No history of dysentery, but lesions *post mortem*, were recorded in 7 or 17.95 per cent., making a total of 71.8 per cent. in which *post-mortem* lesions of dysentery were found. A history of previous dysentery without lesions *post mortem* were recorded in 6 more, or 15.38 per cent., making a total of 87.12 per cent. in which there was either clinical or *post-mortem* evidence or both of dysentery. In 5 or 12.83 per cent. there was neither a history or *post-mortem* evidence of dysentery recorded. If we now add this series to the first one we have a total of 63 cases with complete clinical and *post-mortem* records, in 55.5 per cent. of which there was both clinical and *post-mortem* evidence of dysentery, 20.63 per cent. with *post-mortem* evidence only, making a total of 76.18 with dysentery found at the necropsy, and 14.3 per cent. in which there was clinical, but no *post-mortem*, evidence of previous dysentery, making a total of 90.48 per cent. with either clinical or *post-mortem* evidence of the disease. This leaves only 9.52 per cent. in which no evi-

TABLE III.—*Clinical and Post-mortem Evidence of Dysentery in Liver-Abscess Cases.*

No.	Caste.	Sex.	Age.	Alcoholism.	History of Dysentery.	Duration of Illness.	Temperature.	Number of Abscesses Post Mortem.	Lesions of Dysentery Post Mortem.
1	H	M	40	No	3 years ago	1 year	98° to 100°	1 large, many small	Scars of ulcers in colon.
2	H	M	20	—	6 mos. ago for 3 months	?	99° to 101°	1 large	No ulcers or scars, slight congestion,
3	H	F	38	No	2 years up to 1 year ago	15 months	97° to 98°	1 large	Recent dysentery.
4	H	M	28	Yes	6 months ago	1 month	98° to 100°	1 large, many small	Ulcers (amoebic).
5	H	M	40	No	18 days	3 months	Normal	1 large, many small	Nil.
6	H	M	22	No	1 year ago	13 days	98° to 100°	1 large	Nil, but colon adherent to liver.
7	H	M	30	Yes	1½ month ago	1 month	98° to 102°	1 large	Scars of old ulcers in colon.
8	M	M	36	Yes	2 months ago	1½ month	98° to 101°	1 large	Recent ulceration.
9	H	M	25	—	No history recorded	—	98.4° to 103°	1 small	Nil.
10	H	M	29	Yes	Nil	Not noted	97° to 101°	2 large, many small	Amoebic type of ulcers in caecum.
11	H	M	60	Yes	Not noted	1 month	—	1 large, 2 old ones	Recent dysentery.
12	H	M	40	No	Nil	2 months	Normal	1 large	Ulcers in colon of amoebic type.
13	M	M	30	No	2 years ago	1½ month	97° to 101°	1 large, many small	Recent dysentery in caecum.
14	H	M	50	Yes	1 year ago	1½ month	98.4° to 101°	1 large, loculated	Recent dysentery, ulcers in caecum.

dence of the disease was got, a proportion which can be easily explained on the ground of imperfection of the clinical records and to slight or latent forms of the disease producing no symptoms and healing before death took place.

We may then, I think, conclude that dysentery is constantly, or almost constantly, associated with tropical or amoebic abscess of the liver.

TIME RELATIONSHIP OF DYSENTERY TO LIVER ABSCESS.

It is frequently stated, in objection to the view that liver abscess is secondary to dysentery, that the bowel complaint may occur simultaneously with, or even later than, the abscess, so that the latter cannot be dependent on the former, but at the most both conditions may be due to a common cause. Here once more mere clinical data alone will not serve to decide the point, as dysentery, especially the amoeboid form, may be latent for long periods and then recur, so that a history of dysentery during or after the onset of symptoms of liver abscess by no means precludes the possibility, or even probability, of the bowel disease having also been present in a mild or latent form before the liver affection declared itself. Turning once more to cases in which both clinical and *post-mortem* data are available in the same cases I find in my tabulated and *post-mortem* material 40 cases in which the dates of the attack of dysentery and of the onset of the symptoms of liver abscess are recorded, together with *post-mortem* evidence at a later date. In 32 of these, or 80 per cent., the dysenteric attack preceded the first symptoms of liver abscess, fever accompanied by pain in the hepatic region being taken as indicative of the onset of the liver disease. In 6 of these, however, the history of dysentery was upwards of one year before the commencement of the liver symptoms, and exception might be taken to these as being too remote to be causatively associated with the hepatic disease. On examining the *post-mortem* records of these cases I find that in 3 of them there was evidence *post mortem* of both old and recent dysentery, and in a fourth of recent dysentery only, in one only old dysenteric lesions were found, while in the sixth no lesions were seen *post mortem*. We see, then, that in two-thirds of these cases there was *post-mortem* evidence of recent dysentery, which had not given rise to any symptoms sufficiently definite to be remembered by the patient as an attack of dysentery, or, in other words, although ulcerations were still present in the large bowel and had been so for periods varying from two to ten years (if the histories are to be relied on), yet it had remained in a latent condition and produced no marked clinically evident dysentery. Of the remaining cases the dysentery appeared at about the same time as the symptoms of liver disease in three, or 7.5 per cent., but in all of these there was *post-mortem* evidence of dysenteric ulceration of the bowel of a date certainly antecedent to the liver abscess symptoms. In the remaining five cases, or 12.5 per cent. of the whole, the dysenteric symptoms set in after the symptoms of liver disease, but in three of these again there was *post-mortem* evidence of ulceration of the large bowel of an older date as well as recent lesions. In the other two there were no lesions found in the large bowel or in any other part of the gastro-intestinal tract, in spite of the clinical evidence of quite recent dysentery, so that the lesions must have healed up, and it is equally possible, and, in view of the constancy

of previous dysentery in the vast majority of the cases here dealt with, we might almost say probable, that there had been older dysentery, which had healed in a similar manner without leaving evident naked-eye changes.

Taking the whole series, we find a clear history of antecedent dysentery in 32, or 80 per cent. of the cases, while out of the eight cases in which the dysentery clinically coincided with or succeeded in time the onset of liver symptoms there was *post-mortem* evidence of dysenteric ulceration of a date prior to the liver disease in no fewer than 6, or 15 per cent. This leaves only two cases, or 5 per cent., in which there was not evidence either clinical or *post-mortem* of the dysentery having preceded in time the liver abscess, and even in these it is impossible to be certain that it did not do so, while in 95 per cent. positive evidence of preceding dysentery was obtained.

THE TYPE OF DYSENTERY IN LIVER ABSCESS CASES.

The variety of dysentery which is associated with the tropical form of liver abscess remains to be considered, my own experience being again first related, and the older *post mortem* records appealed to for confirmation or otherwise of the conclusions arrived at. Turning once more to Table II, we can note the type of dysentery met with in a series of cases of liver abscess which have been proved to contain amoebae in their walls. Unfortunately, in two of the earlier cases no microscopical examination of the ulcers for amoebae was made, while the same remark applies to No. 13, owing to the case occurring during my temporary absence. This leaves 8 cases in which actual ulceration was found *post mortem* in which the amoeba was sought for, and in each of them this organism was easily found in large numbers in the yellow material in the bases of the ulcers, not infrequently being so numerous as to be seen in every field of the microscope with a $\frac{1}{6}$ in. lens in an active condition. Further, I have only twice met with this form of dysentery *post mortem* in other than fatal liver abscess cases. In one of these there was a postcolic abscess due to perforation of an amoebic ulcer, and the colon was adherent to the liver, and pus was just beginning to infiltrate the liver substance at the point of contact, forming the earliest stage of a liver abscess. The remaining patient died of phthisis. That this form of dysentery is really quite distinct from the ordinary Indian dysentery will be evident from the fact that an officer of the Indian Medical Service, who had had many years' experience of dysentery in Indian gaols where necropsies are always performed, to whom I recently showed several excellent coloured drawings made from my cases, said that he had never seen that kind of dysenteric ulcer before. He had only just before remarked that liver abscess was so rare in gaols that he did not see how it could be associated with such a common disease as gaol dysentery. Although, then, the number of my own necropsies is not very great in liver abscess cases, yet it very clearly points to the tropical or amoebic liver abscess being associated exclusively with the less common amoebic variety of dysentery, this form being rarely met with apart from liver abscess or other intra-abdominal abscess secondary to amoebic perforation of the large bowel.

On turning to the more extensive older *post-mortem* records for confirmation of this conclusion much greater difficulties

are met with than in merely deciding if dysentery had been present, and its probable date, for even where the descriptions of the lesions found are fairly complete, it is by no means easy to form an accurate mental picture of the condition from a written description of it. Still, my experience of the conditions found in the cases which I have proved to be amoebic by microscopical examination has enabled me to recognize at once in the records of many necropsies on liver abscess cases a faithful description of amoebic dysentery, while contemporaries of Dr. McConnell have informed me that that excellent observer recognized the dysentery associated with liver abscess as being different from the ordinary form of the disease, although I have not been able to find any description of it by him. On going through the records of 95 cases in which some description of the condition of the large bowel in liver abscess cases was recorded I was able to recognize 50 of them as accurate descriptions of the conditions I have met with in true amoebic dysentery, that is, in a little over one-half of the cases. In 19 more I noted as being "probably amoebic," making a total of 72 5 per cent. as pretty certainly or probably of this type. In 23 I was unable to form any opinion and entered them as doubtful, while in 3 only the conditions described appeared to me to more closely resemble the ordinary type than the amoebic variety, although they were not incompatible with the very catholic description of amoebic dysentery by Lafleur. Allowing for the great difficulty in arriving at a correct and unbiassed opinion from the data dealt with I still think that these figures strongly confirm the conclusions derived from the smaller number of carefully observed cases recorded in Table II, especially when we bear in mind the rarity with which the amoebic form of dysentery has as yet been met with in India, apart from tropical liver abscess, the only possible conclusion appears to me to be that the form of dysentery associated with, and as we have already seen nearly, if not quite, invariably preceding the amoebic form of liver abscess is the variety produced by the amoeba dysenterica.

In support of this view I may also mention that in 17 cases of multiple small pyaemic abscesses of the liver without any large abscesses of which I have been able to examine the *post-mortem* records, in no fewer than 14 the dysentery was clearly of the ordinary catarrhal as opposed to the amoebic variety; in 2 no definite opinion could be formed, while in 1 the condition described appeared to be possibly of the amoebic variety. The multiple small pyaemic liver abscess, then, is associated with severe forms of ordinary dysentery, and in nearly all of these cases in which clinical records are also available I find the patients were admitted and treated for severe dysentery, and the pyaemic abscesses of the liver were not diagnosed, although in one or two cases some tenderness in the hepatic region was noted. On the other hand, in the "tropical" or amoebic abscess cases the patients are clinically diagnosed as liver abscess in the vast majority of the cases, and are comparatively rarely admitted for dysentery. In other words, liver abscess as recognized and treated clinically in the tropics is in the vast majority of cases of the tropical or amoebic variety, and is preceded in a very large percentage of the cases by dysentery of the amoebic type.

THE SEASONAL INCIDENCE OF LIVER ABSCESS IN RELATION TO THE TYPE OF DYSENTERY.

The month of admission for liver abscess has been worked out from 236 cases in order to see what is the seasonal variation of the disease. Arranging the figures in quarterly periods we arrive at the following results: In the first quarter of the year, January to March, there were 59 cases; in the second quarter, from April to June, there were 58; in the third, from July to September, there were 58, and in the last quarter, from October to December, there were 61. These figures show that there is no season of special prevalence of the disease—a fact which is of great interest in relation to the kind of dysentery which is associated with liver abscess, as it is in entire agreement with the conclusion that this form is the amoebic one, for, owing to the chronicity and frequent latency of amoebic dysentery, and the way in which it relapses again and again through several years, there is no definite seasonal prevalence of the disease. On the other hand, the ordinary catarrhal or membranous dysentery has a most definite seasonal incidence, which is usually coincident with that of malaria, reaching its maximum during and after the rainy season, so that if liver abscess was associated with this form of the disease it should also have a seasonal incidence closely following that of catarrhal dysentery, which we see is not the case. It is also of interest to note in this connexion that multiple pyaemic abscesses following severe sloughing catarrhal dysentery most frequently occurred in the latter half of the year, which is the season of greatest prevalence of the ordinary form of dysentery, while nearly half of them occurred in August and September, when the dysentery season is at its height, thus confirming the relationship of the multiple small pyaemic liver abscess with the common catarrhal form of dysentery.

OTHER ETIOLOGICAL FACTORS.

There is a very general belief that alcohol plays a very important part in the etiology of liver abscess, and this opinion is borne out by the fact that in more than half the cases in my tables in which this point was noticed a history of alcoholism was obtained, although it is not easy to say whether actual excess or only very moderate amounts are indicated in some of the notes. Alcohol, then, appears to be an important predisposing cause of the disease. On the other hand, I have not been able to find any evidence of malaria predisposing to the disease, for although a previous history of so-called malarial fever is often noted, this is usually but the intermittent fever of hepatitis. The *post-mortem* records show that the spleen is seldom enlarged or pigmented in tropical liver abscess, not oftener than in those dying of other non-malarious disease in Lower Bengal.

AMOEBIC DYSENTERY.

It is beyond the scope of the present paper to describe in detail the lesions produced by amoebic dysentery as seen in India. The main naked-eye features of the disease may, however, be briefly mentioned. Writing with five coloured drawings made from my cases before me, one is struck by the difference in appearance between the very large ulcers, several square inches in extent, with yellowish white sloughy surfaces, which are met with exclusively in some cases, and

the small ones which alone are found in others, which in one case were little larger than a big pin's head. Every degree of these changes, however, is shown in the coloured drawing [exhibited], taken from a case of very large single abscess of the liver in a European patient. The caecum and ascending colon are covered with raised yellowish white sloughy gelatinous material forming very extensive ulcers, with only small areas of healthy mucous membrane between them. The unaffected portions are bounded by well-marked raised borders of the ulcerated patches, and a thin dark purple line of intense congestion is seen at their boundaries. Thus the ulcers form the raised thickened patches, and the healthy mucous membrane between is of normal thickness, appearing to be depressed below the level of the diseased portions. This, which is just the opposite of the condition met with in the ordinary form of dysentery, is to my mind the most characteristic feature of the amoebic dysentery. The lowest of the large ulcers shows very well the clear line of demarcation between the healthy and diseased portions of the mucous membrane with its thin purple congested zone. Below this will be seen the smaller form of ulcer, which is that most frequently met with in these cases in my experience. The larger of these are of an oval shape extended across the long axis of the bowel, and usually placed on the summits of folds of the mucous membrane in the form of raised patches with a well-defined margin, often showing a ring of congestion, and with a pale yellow surface constituted by the gelatinous infiltration of the submucous coat appearing in the centre of the ulcer on account of the mucous membrane having become detached. The smaller of these are rounded in form, and have thickened edges formed by the mucous membrane being raised by the infiltration beneath it, this material again appearing as pale yellow purulent matter in the centre of the ulcer, the whole being usually surrounded by a distinct narrow zone of congestion. These ulcers may be very few in number, or they may be scattered over the surface of the greater length of the large bowel. Between the small raised patches and ulceration the unaffected mucous membrane appears to be quite healthy, or only shows slight congestion, and, except in very chronic cases, there is no general thickening of the whole of the mucous membrane of the bowel, which is so characteristic of the ordinary catarrhal form of dysentery, and this no doubt accounts for the frequent absence of tenesmus and the common latency and entire absence of dysenteric symptoms in the amoebic disease.

Lastly, the ulcers may be very small, appearing as red dots, in the centre of which, on close observation, a minute pale-yellow superficial ulceration can be detected, surrounded by a red ring of congestion. Such are the general characters of amoebic ulcers of the large intestine, but in some cases a few of the ulcers may show excavation due to loss or separation of the yellow material, and may then present a somewhat greyish appearance. Others may show a shallow excavated surface with a hard slightly raised border, these being in the stage of slightly slow healing. In some very chronic cases all that will be found may be narrow oval or slit-like depressions, with very thick slightly raised overhanging borders with none of the characteristic yellow matter, and with very hard fibrous bases, evidently chronic half-

healed ulcers, but even in this stage amoebae may be found in the floors of the ulcers, as in Case 2 of Table II.

The distribution of the disease in the large bowel is also of great importance, for in my experience, in all cases where more than a few small ulcers are present the caecum is most markedly affected, and next to it the ascending colon suffers most, the disease being frequently nearly or quite limited to these parts of the large bowel, especially in those cases where no symptoms of dysentery have been present during life. The largest form of ulcer is commonly limited to the caecum or to this and the ascending colon, while the smaller ones frequently extend considerably lower down, but do not as a rule affect the sigmoid flexure or rectum. This distribution of the ulcers, together with the absence of thickening or inflammatory changes between the ulcers, constitutes the most characteristic features in which amoebic dysentery differs from the ordinary catarrhal or membranous form of the disease. Lastly, the amoeba dysenterica is very easily found in the floors of the ulcers, the yellow infiltration often showing numerous active amoebae in every field of the microscope.

It should also have been mentioned that although the caecum is so markedly affected, the disease is strictly limited by the ileo-caecal valve, and does not invade the lower few inches of the small intestine, as is so often seen in catarrhal dysentery. Chronic peritonitis is not infrequently associated with amoebic dysentery, while the large bowel, and especially the hepatic flexure of the colon, is often adherent to the liver. In one case the large loop of the small intestine was strangulated by a band resulting from such chronic peritonitis, and in the same case a liver abscess opening into the stomach was found containing amoebae. Quite recently a case of acute peritonitis due to perforation of an amoeboid ulcer of the vermiform appendix has been met with, a very large single liver abscess being also present, the amoebae were found in the liver abscess wall in the perforated ulcer, and in both the large and small ulcers in the large intestine.

This tendency to the production of chronic peritonitis and adhesions is a marked feature of amoebic dysentery, and is produced by a spread of the disease process through the wall of the bowel, without, as a rule, any actual perforation taking place. This feature of the disease is of great importance in connexion with the mode of production of the single large abscess in the liver following amoebic dysentery, for it is scarcely possible to explain this by the passage of the amoebae through the portal vein, for such a mode of infection would surely produce multiple abscesses in the vast majority of the cases, instead of the opposite being the case. Lafleur has recorded the fact that the amoeba dysenterica has been found in the peritoneal cavity without any actual perforation of the bowel; and when we remember the way in which an amoebic abscess of the liver will burrow through the diaphragm into the lung or pericardium, it is not surprising that it may pass through the wall of the large bowel. Once in the peritoneum, the circulation within this cavity would tend to carry it slowly but surely towards the large lymphatics under the diaphragm, and, being stopped here by the suspensory ligament of the liver, it might work its way into the organ at this point, thus accounting for this place being the commonest seat of single liver abscess. I have been struck by the fact that even com-

paratively small amoebic abscesses are nearly always situated just under the surface of the organ, and are rarely deep in its substance at all points of their circumference—a fact which is easily explained on this supposition. The frequency with which the ascending colon and hepatic flexure shows marked amoebic ulceration may also account for the disproportionate affection of the neighbouring right lobe of the liver, even allowing for its greater size. In this way the frequency with which perihepatic abscess was associated with amoebic dysentery in the Calcutta *post-mortem* records is also easily explained, this form of the disease being generally of the same nature as the amoebic abscess of the liver, while both conditions were met with together in several cases of great interest, a point which space does not permit of elaboration here.

THE VALUE OF LEUCOCYTOSIS IN THE DIAGNOSIS OF LIVER ABSCESS.

I have elsewhere⁴ dealt with this point, but as it is completely overlooked in some otherwise excellent accounts of liver abscess, while attention to it will save many serious mistakes, I wish to give one more recent example of its value. A brief experience of tropical work will suffice to teach the difficulty of diagnosis between intermittent malarial fevers and the intermittent fever which is the usual precursor of liver abscess; many a man who has been sent on a sea voyage for the treatment of the former having developed the latter condition. Recently I was asked to examine the blood of a patient who was being treated for malaria, the parasites having been thought to have been detected in his blood. The first glance at the edge of my stained slide showed a great excess of leucocytes, about 90 per cent. of which proved to be polynuclears, leucocytosis being evidently present, a supposition which was confirmed by a count on the following morning. At this time quinine was being given in full doses hypodermically, but the fever was getting higher, and had become of a remittent type. It was now found that he had suffered from pain over the liver and in the right shoulder. However, he was sent on a voyage to Colombo a few days later, my opinion that the case was one of liver abscess and not malaria not having been accepted. At Colombo a liver abscess was opened. The reverse of this happened in another case of fever with signs of hepatitis, in which I was asked to examine for leucocytes. I found them decreased to 2,250 per c.mm., 21 per cent. of which were large mononuclears, these changes being characteristic of malaria, as I have shown elsewhere.⁵ A further search revealed malignant tertian parasites. In my experience leucocytosis is most marked in comparatively small deeply-seated abscesses of the liver, in which 30,000 to 40,000 white corpuscles per c.mm. may be found, and less in those which are already beginning to come to the surface, or are forming bulging swellings, probably due to the lower tension in there, as is so often the case with natives when first admitted. That is, this change is most marked just in those cases where the diagnosis is most difficult, and in which leucocytosis will exclude malarial fever. In one recent case, which proved to be a very

⁴ *Proceedings of the Nagpore Malarial Conference.*

⁵ *BRITISH MEDICAL JOURNAL*, 1902, i, p. 827.

large single liver abscess, only 8,625 leucocytes were found per c.mm., but the red only numbered 2,860,000, so that the proportion of white to red was 1 to 332, or twice the normal, and this is the lowest count I have yet met with in liver abscess cases.

THE ACTION OF QUININE ON AMOEBA AND ITS BEARING ON THE TREATMENT OF LIVER ABSCESS.

Finally, I come to the practical application of the conclusion that "tropical liver abscess" is produced solely by the amoeba dysenterica. Lafleur states that quinine in a solution of 1 in 5,000 will kill this organism, and injections of the drug are used in the treatment of amoebic dysentery. This suggested to me that cases in which thick liver abscess pus swarming with living amoebae continued to be discharged for days after the abscess had been opened, evidently owing to continued breaking down of the liver substance, might be benefited by washing out the cavity with quinine solutions. Such a case was 14 of Table I, in which on the ninth day after the abscess had been opened and efficiently drained, there was thick discharge swarming with amoebae, together with fever and continued loss of strength. I suggested washing out the abscess cavity with a 1 in 500 solution of quinine, with the result that in two or three days the thick discharge was replaced by a thin, almost serous, one, and the patient began to improve from that time, and made a good recovery. A very similar result was obtained in Case 2, Table I, in which the injections were commenced on the eighth day after opening, the discharge being then still thick and copious, and within two days it had become much less, and subsequent progress was very favourable. This treatment is only of use as long as amoebae are present in the discharge.

Experiments were then carried out to ascertain what strength of quinine is required to kill the amoebae found in liver abscess cases, those from several different cases being used, scrapings from the abscess wall obtained either during life or *post mortem*, being mixed with quinine in normal saline solution, both the neutral soluble bi-sulphate and the ordinary sulphate (1 grain to 1 minim of dilute hydrochloric acid) being tested, controls of the pus diluted equally with normal saline solution being always used. As the temperature of the laboratory during these experiments was over 90°F. the use of a warm stage was unnecessary. Without giving all the details of the experiments it may be said that 1 in 1,000 quinine solution (both soluble and insoluble salts) failed to destroy the amoeba even after several hours contact, having apparently little more effect than normal saline solution. On the other hand, 1 in 500 solutions stopped all movement of the amoeba in from five to fifteen minutes as a rule, a temporary stimulating effect being sometimes first observed. In order to test if such a strength would be effective when applied to the wall of a living abscess a piece of such a tissue, which was full of active amoebae, was placed in a solution of 1 in 500 sulphate of quinine in normal salt solution, and scrapings examined every five minutes. In none of them were any living amoebae found. In another trial some of the amoebae in a thick abscess wall survived the action of a 1 in 500 quinine in normal saline solution for one hour, but were destroyed and rendered granular by a 1 in 100 solution in five minutes, while this last strength in distilled

water killed them at once. A 1 per cent. solution, then, appears to be an efficient destructive agent of the amoeba in the wall of a liver abscess, although an even stronger solution might be advisable on account of the difficulty of its diffusion through the very tenacious pus of a liver abscess.

But if such a solution of quinine will destroy the amoeba in the wall of an abscess which has been opened when the cavity is merely washed out with it, and the fluid allowed to run out again, will it not have a still more marked action if injected into the cavity of the abscess after as much as possible of the pus has been removed by aspiration, and left there to saturate the wall in which the amoeba is found in its active condition? Such a line of treatment appears to me to be the logical outcome of the proof that the amoeba is the sole constantly met with organism in tropical liver abscess, and without fully elaborating the argument here the following facts may be urged in support of this suggestion. In the first place it is well known that this form of abscess of the liver is not very infrequently cured by one or more aspirations without being opened at all, several such cases having occurred at the Medical College Hospital, Calcutta, during the last few years, while a number could be collected from the pages of the *Indian Medical Gazette* and other journals. Further, it is also a fact that these abscesses may become encysted and dried up to a caseous or putty-like mass without any treatment at all, and this is a less uncommon event than might be thought, for I have come across 8 such cases in the Calcutta *post-mortem* records, in 1 of which there was also a recent abscess as well.

Although such cases occur, still in the great majority of liver abscesses only temporary benefit is obtained from a simple aspiration, and on being subsequently opened active amoebae are found, which account for the recurrence of the pus formation, for we have seen that in the great majority of freshly-opened abscesses no staphylococci are found. If, then, the great bulk of the pus is removed by aspiration and the amoebae are killed by an injection of quinine solution, why should not some at least of these abscesses encyst or become absorbed, as occasionally occurs in the natural course of the disease, and more frequently still after the simple removal of the pus by aspiration? This would especially apply to the smaller and deeply-seated abscesses, which are just those in which aspiration has to be performed for the purpose of diagnosing and locating the disease before any operation for opening them is undertaken. Why should not the quinine solution be injected at this time, the pus which has been removed being examined by the microscope and cultures for pus-forming cocci, and if these are absent the case might safely be watched for a time to see if the abscess will subside after the quinine injection? The dose might be 30 gr. or more of quinine dissolved in from 2 oz. to 5 oz. of water and sterilized; the lesser quantity being used in small abscesses containing only about 10 oz. of pus, and the full amount in larger ones, so as to bring as concentrated a solution into contact with the collapsed abscess wall as the limited dose will allow of, and at the same time permit sufficient of the solution being used to saturate the whole extent of the wall of the cavity. The ordinary insoluble sulphate (1 gr. to 1 minim of acid sulph. dil.) would probably be best as being less likely to be rapidly absorbed from the cavity, although I do

not think there is much likelihood of this interfering materially with the effect of the solution, on account of the very densely fibrous nature of the walls of most of these abscesses; 30 gr. of quinine in 5 oz. of water will make a strength of 1 in 80, which is more than that required to kill the amoeba quickly, while if a 30-gr. dose be used in 2 oz. or 3 oz. a still stronger solution can be injected. This method is about to be tried in Calcutta, and I hope before long to be able to report on it.

CONCLUSIONS.

1. The amoeba is constantly found in an active condition in the wall of tropical abscess of the liver, although frequently absent from the pus in its cavity. The amoeba is the only organism constantly found in such abscesses.

2. Staphylococci and other pyogenic bacteria are absent from the pus in the great majority of cases when the abscess is first opened.

3. In cases of which a complete record is available there is either a history of dysentery or lesions of this disease are found *post mortem* in over 90 per cent. of the cases, and it cannot be certainly excluded in the remainder.

4. The dysentery precedes the liver abscess or lesions in the large bowel of an antecedent date and are found *post mortem* in 95 per cent. of the cases.

5. The form of bowel disease associated with the large tropical or amoebic abscess of the liver is amoebic dysentery.

6. Severe sloughing forms of catarrhal dysentery may be associated with small multiple pyaemic abscesses, which is a totally distinct condition from tropical or amoebic abscess, and is very rarely recognized during life.

7. Quinine solutions rapidly destroy the amoeba, and may be used with advantage in washing out liver abscesses after they have been opened. They are also worthy of a trial as injections after aspiration of the pus as a possible curative measure, especially in such cases as are found to be free from the ordinary pyogenic organisms.

WELLCOME INSTITUTE LIBRARY	
Coll.	welMOMec
Coll.	pam
No.	WI 700
	1902
	R 72 t